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REMARKS

Claims 15 and 17 have been canceled without prejudice. Claims 1, 16, and 59 have been amended. Support for amended claims 1 and 59 can be found in originally filed claims 15 and 17. No new matter has been introduced and no new issue has been raised. These amendments have been made solely to expedite allowance. Applicants reserve the right to pursue claims of similar or differing scope in the future.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Elections/Restrictions

Applicants continue to traverse the restriction requirement and reiterate the arguments already made of record. Applicants state the claimed invention relates to a genus of nucleic acid compounds that decrease the expression of EphB4 in a cell rather than a species. Applicants argue it is inappropriate for the Examiner to restrict the claimed invention to an un-recited species in a genus claim.

Claim Objections

Claims 15-17 are objected to as being dependent upon a rejected base claim and reciting non-elected subject matter, but, according to the Examiner, would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and deleting non-elected subject matter. Applicants respectfully disagree with the objection, but it an effort to expedite prosecution have amended claim 1 to incorporate the features of claims 15 and 17. Applicants respectfully request reconsideration and withdrawal of this objection.

Claim Rejections – 35 USC § 102 or 35 USC § 103

Claims 1, 3, 5-7, 9-11, 13 and 59 are rejected under 35 U.S.C. 102(b) or 35 U.S.C. 103(a) as being anticipated by or obvious over Bennett et al. (Patent No: 6,277,640). Applicants traverse this rejection to the extent it is maintained over the claims as amended.

Independent claim 1 as amended recites an isolated nucleic acid compound comprising at least a portion that is complementary to at least 15 contiguous nucleotides of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases the expression of EphB4 in a cell, wherein the nucleic acid compound is an isolated nucleic acid compound, and the antisense nucleic acid compound comprises one or more modified backbone or base moieties and comprises at least one 2'O-alkylated ribonucleotide.

The standard for anticipating a claim is clearly outlined in MPEP 2131, and this standard is further supported by the Courts. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631 (Fed. Cir. 1978).

Applicants contend that Bennett et al. fail to satisfy the criteria for anticipating the present invention. Bennett et al. describe antisense compounds for modulating the expression of CD44. Bennett et al. do not teach or suggest compounds for decreasing the expression of EphB4. More specifically, Bennett et al. fail to teach or suggest an antisense nucleic acid compound comprising at least one 2'O-alkylated ribonucleotide. Accordingly, Bennett et al. do not teach all the elements of independent claims 1 or 59 and fail to anticipate claims 1 and 59. For the same reasons, Applicants submit that all claims depending from claim 1 or 59 are not anticipated by Bennett et al.

Applicants further submit that Bennett et al. do not render obvious the instant claims and note that pursuant to MPEP 2142, "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)."

The instant claims relate to nucleic acid compounds for decreasing the expression of EphB4, whereas Bennett et al. are concerned with modulation of the expression of CD44. Indeed, Bennett et al. are absolutely silent on EphB4 as a target for antisense compounds. Bennet et al. are also silent regarding antisense compounds that comprise a specific 2'O-alkylated ribonucleotide modification. In the absence of any suggestion in the cited art that EphB4 gene expression should be targeted for inhibition, one of skill in the art would not have been motivated to make EphB4 targeted nucleic acids as claimed in this application.

Claims 1, 3, 5-8, 10-11, 13 and 59 are rejected under 35 U.S.C. 102(e) or 35 U.S.C. 103(a) as being anticipated by or obvious over Khvorova et al. (US 2005/0246794). Applicants traverse this rejection as it is maintained over the claims as amended. Applicants contend that Khvorova et al. fail to satisfy the criteria for anticipating the present invention. Khvorova et al. describe methods for increasing siRNA efficacy and do not teach or suggest compounds for decreasing the expression of EphB4.

The amended claims recite an isolated nucleic acid compound that decreases the expression of EphB4 in a cell comprising at least a portion that is complementary to at least 15 contiguous nucleotides of SEQ ID NO: 392 and comprises at least one 2'-O-alkylated ribonucleotide. Khvorova et al. provide over 159,000 sequences. Paragraphs [135]-[138] of the cited document recite long lists of nucleotide analogs, including those with modifications of the base, sugar, and or phosphate group. As the compound in the instant application is not specifically named, but in fact can only be provided by selecting specific portions of the teaching and combining them, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. Ex parte A, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). As one of ordinary skill in the art is not able to "at once envisage" from Khvorova et al. the compound in the instant application, the compound is not anticipated.

Accordingly, Khvorova et al. do not teach all the elements of independent claim 1 or 59 and fail to anticipate claims 1 and 59. For the same reasons, Applicants submit that all claims depending from claim 1 or 59 are not anticipated by Khvorova et al.

Applicants further submit that Khvorova et al. do not render obvious the instant claims. The instant claims relate to antisense nucleic acid compounds for decreasing the expression of EphB4, whereas Khvorova et al. are concerned with methods for increasing siRNA efficacy. Khvorova et al. disclose siRNAs against a number of targets including cyclophilin, human DBI, firefly luciferase, renilla luciferase, human PLK, human secreted alkaline phosphatase, Eg5, GADPH, ATE1, MEK2, MEK1, QB, c-myc, and bcl-2. However, Khvorova et al. are absolutely silent on EphB4 as a target for inhibition. In the absence of any suggestion in the cited art that the EphB4 gene expression should be targeted for inhibition, one of skill in the art would not have been motivated to make EphB4 targeted nucleic acids as claimed in this application.

Claims 1, 3, 5-8, 10-11, 13 and 59 are rejected under 35 U.S.C. 102(e) or 35 U.S.C. 103(a) as being anticipated by or obvious over Robbins et al. (Patent No: 6,770,633). Applicants traverse this rejection.

Robbins et al. are concerned with treating proliferating eye and skin diseases. In particular, they disclose ribozymes useful in this treatment. The SEQ IDs cited by the Examiner in the attached sequence alignment (namely SEQ ID NOs 72 and 73) are in fact ribozyme recognition sites, see Table 17 of Robbins et al. Robbins et al. fail to teach or suggest isolated nucleic acid compounds complementary to at least 15 contiguous nucleotides of an EphB4 transcript and further comprises at least one 2'O-alkylated ribonucleotide. Accordingly, Robbins et al. do not teach all the elements of independent claim 1 or 59 and fail to anticipate claims 1 and 59. For the same reasons, Applicants submit that all claims depending from claim 1 or 59 are not anticipated by Robbins et al.

Applicants further submit that Robbins et al. do not render obvious the instant claims. The instant claims relate to nucleic acid compounds for decreasing the expression of EphB4, whereas Robbins et al. are concerned with methods of treating proliferative eye disease using ribozymes, i.e., catalytically active RNA. In addition, Robbins et al. are absolutely silent on EphB4 as a target for inhibition. In the absence of any suggestion in the cited art that the EphB4 gene expression should be targeted for inhibition, one of skill in the art would not have been motivated to make EphB4 antisense nucleic acids as claimed in this application.

Claims 1, 3 and 14 are rejected under 35 U.S.C. 102(e) or 35 U.S.C. 103(a) as being anticipated by or obvious over Venter et al. (Patent No: 6,812,339). Applicants traverse this rejection. Applicants contend that Venter et al. fail to satisfy the criteria for anticipating the present invention. Venter et al. disclose polymorphic, SNP containing nucleic acid sequences. Venter et al. do not teach or suggest compounds for decreasing the expression of EphB4. More specifically, Venter et al. fail to teach or suggest an isolated nucleic acid compound that is complementary to at least 15 contiguous nucleotides of an EphB4 transcript and further comprises at least one 2'O-alkylated ribonucleotide. Accordingly, Venter et al. do not teach all the elements of independent claim 1 and fail to anticipate claim 1. For the same reasons, Applicants submit that all claims depending from claim 1 are not anticipated by Venter et al.

Applicants further submit that Venter et al. do not render obvious the instant claims. The instant claims relate to nucleic acid compounds for decreasing the expression of EphB4, whereas Venter et al. are concerned with identifying SNPs in genes that contribute to human disease. Venter et al. are absolutely silent on EphB4 as a target for inhibition. In the absence of any suggestion in the cited art that the EphB4 gene expression should be targeted for inhibition, one of skill in the art would not have been motivated to make EphB4 antisense nucleic acids as claimed in this application.

Accordingly, none of the references cited by the Examiner, taken alone or in any combination teach or suggest the isolated nucleic acids as claimed in the instant application. Reconsideration and withdrawal of the rejection are respectfully requested.

Response to Applicant's Arguments Claim Rejections – 35 USC § 112

The Applicant notes that the rejection of record of claim 29 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement has been withdrawn in response to claim amendments filed August 7, 2006.

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Application No. 10/800,077 Docket No.: VASG-P01-001

Response to Applicant's Arguments Claim Rejections – 35 USC § 102 or 35 USC § 103

The Applicant notes that the rejection of record of claims 1-7, 9-13 and 59-60 under 35 U.S.C. 102(b) or 35 U.S.C. 103(a) as being anticipated by or obvious over Bennett et al. has been withdrawn in response to claim amendments filed August 7, 2006.

The Applicant notes that the rejection of record of claims 1-13, 26-29 and 59-60 under 35 U.S.C. 102(b) or 35 U.S.C. 103(a) as being anticipated by or obvious over Pavco et al. (Patent No: 6,346,398) has been withdrawn in response to claim amendments filed August 7, 2006.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (617) 951-7000. If a fee is due, please charge our Deposit Account No. 18-1945, under Order No. **VASG-P01-001**.

Dated: April 27, 2007

Respectfully submitted,

Reg No. 46,778

By for Z. Angela Gao, Ph.D.
Registration No.: 54,144
FISH & NEAVE IP GROUP, ROPES & GRAY LLP
One International Place
Boston, Massachusetts 02110-2624
(617) 951-7000
(617) 951-7050 (Fax)
Attorneys/Agents For Applicant